93. Melanoma antigens or tumor associated antigens isolated by screening candidate antigens according to a method for determining or isolating Class II tumor associated antigens, said method comprising the steps of:

(a) contacting a candidate antigen with antigen presenting cells for a time sufficient to allow the antigen to be processed by said antigen presenting cells;

(b) contacting said antigen presenting cells from step (a) with $CD4^+$ T lymphocytes; and

(c) screening for recognition of said antigen presenting cells by said $CD4^+$ T lymphocytes.

REMARKS

Applicants respectfully request entry of the instant amendment.

In compliance with the Examiner's request, applicants provide a supplemental FORM PTO-1449 providing the month and year for Genbank Accession Nos. J03581, U101873, Y00819, M27160 and EMBL Accession No. M33295 (attached hereto).

Support for the new claims is found in the application as originally filed as follows.

Claim 65: Original claims 1 and 2 and Figure 9.

Claim 66: Original claim 5 and Figure 6.

Claim 67: Original claim 5 and Figures 6 and 9.

Claim 68: Original claims 10 and 12-16.

Claims 69-71: Original claims 17 and 18.

Claims 72-76: Original claims 19 and 20.

Claims 77-79 Original claims 21 and 22.

Claims 80-85: Original claims 23-26.

Claims 86-91: Original claims 27-30.

Claim 92: Original claims 56, 23 and intervening claim 52.

Claim 93: Original claim 61 and claim 57 on which claim 61 depends.

Claims 3-30, 56, 61 and 64 stand rejected under 35 U.S.C. 112, first paragraph. The Examiner contends that "it is reasonable for a skilled artisan in the art to conclude modifications of a peptide will affect the biological activity of said peptide." The Examiner cites Salgaller et al. and Parker et al. in support of this statement.

Applicants do not disagree that modifications of a peptide can affect the biological activity. One does not have to go beyond the instant application to establish that fact. For example, Figure 6 shows the L65→V modification of Ty 56-70 affects biological activity. Further, Figure 9 shows modification by successive removal of amino acids from Ty 448-462 affects biological activity. However, applicants do disagree with the Examiner's Section 112, first paragraph rejection based on the theory that modifications of a peptide, which are described and enabled by the instant specification, require undue experimentation to identify. It is unclear how this can be a basis for a Section 112 rejection.

The Examiner contends that "[d]ue to the unpredictable nature of which modifications are useful (see Lazaret et al., Burgess et al., Sallgaller et al., Parker et al. and Englehard) and the multitude of derivatives encompassed in the claimed invention one skilled in the art cannot practice the invention as claimed absent undue experimentation." Applicants respectfully disagree with these grounds of rejection.

First, the Examiner classifies the instant disclosure as unpredictable in nature and cites several references in support. Certainly, relying on the cited references (relating to MHC Class I molecules) for guidance to produce a MHC Class II immunogenic derivative of tyrosinase may afford unpredictable results. However, the fact is, the references cited by the Examiner support applicants' position of patentability of the instant claims. Englehard states on page 18 that "[p]eptide binding motifs [based on modification of peptides affecting biological activity] have . . . been used to successfully predict peptide epitopes recognized by preexisting T-cell clones from the sequence of the intact protein. However, of even greater importance has been the utilization of motifs and binding assays to identify peptides that can elicit CTL responses of potential therapeutic value." The predictability is based upon numerous examples of modifications that either increased or decreased biological activity of MHC Class I molecules. Such examples, relating to MHC Class II immunogenic derivative of tyrosinase, are found in the instant specification leading one of skill in the art to conclude that utilization of the motifs set forth therein describe peptides of potential therapeutic value.

Therefore, when one wishes to produce MHC Class II immunogenic derivatives of tyrosinase one must look to the instant specification which does provides sufficient guidance to one skilled in the art to practice the invention as claimed. The specification provides numerous examples of peptides and simple methods for assaying for biological activity (Examples I and II).

Further, a significant amount of direction for providing MHC Class II immunogenic derivatives of tyrosinase is given, *inter alia*, in Example II. For example, favorable and unfavorable substitutions and the P1 and P6 anchor positions are identified. In

addition, modifications that enhance and modifications that diminish T cell response are identified. It is clear that there is sufficient guidance in the instant specification for one of skill in the art to practice the invention as claimed. The presence of possibly inoperative embodiments within the scope of the claims does not necessarily render the claims nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Power Co. v E.I. duPont de Nemous & Co.*, 750 F.2d 1569, 1577 224 USPQ 409, 414 (Fed. Cir. 1984). Since applicants have shown that the peptides are readily available and screening them requires no more effort than is normally required in the art the claims are not unduly broad.

It is well established law that even "an extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d at 224, 195 USPQ at 153. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). It is clear that the instant specification gives sufficient direction and guidance and, therefore, the claims are fully enabled.

In light of the above amendments and remarks, applicants respectfully request reconsideration and withdrawal of the Section 112, first paragraph rejection. The instant claims are believed in condition for allowance, and early and favorable action by the Examiner is

earnestly solicited. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 415-8565.

AUTHORIZATION

No additional fee is believed to be necessary.

The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2026-4205.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2026-4205. A DUPLICATE OF THIS SHEET IS ATTACHED.

Respectfully submitted,

MORGAN & FINNEGAN, L.L.P.

Dated: October 29, 1998

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